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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,801	05/30/2001	John W. Cherwonogrodzky	3929-3	5677

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EXAMINER
FORD, VANESSA L

ART UNIT	PAPER NUMBER
1645	13

DATE MAILED: 01/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/866,801	CHERWONOGRODZKY, JOHN W	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 30-53* is/are pending in the application.

4a) Of the above claim(s) *1-12* is/are withdrawn from consideration.

5)☒ Claim(s) *44,52 and 53* is/are allowed.

6)☒ Claim(s) *30-43 and 45-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 18, 2002 has been entered.

2. Applicant's amendment is acknowledged. Claims 30, 43, 46 have been amended. Claims 47-53 have been added.

3. The text of those sections of the Title 35, U.S. code not included in this action can be found in the prior Office Action.

Rejections Withdrawn

4. In view of Applicant's amendment and response the following rejections are withdrawn:

a) Rejection of claim 45 under 35 U.S.C. 112, first paragraph on pages 3-5, paragraph 4 of the previous Office action.
b) Rejection of claims 30-41 and 45-46 under 35 U.S.C. 102(b) on pages 11-13, paragraph 8 of the previous Office action.
b) Rejection of claims 30-34, 41, 44 and 46 under 35 U.S.C. 102(b) on pages 13-14, paragraph 9 of the previous Office action.

Rejections Maintained

5. The rejection under 35 U.S.C. 102(b) as anticipated by Pasarell et al is maintained for claims 30-36, 40-41 and 45-46 for the reasons set forth on pages 5-7, paragraph 5 of the previous Office Action.

The rejection was on the grounds that Pasarell et al teach concentrated culture filtrate antigens that were obtained from the genera *Alternaria, Bipolaris, Curvularia, Dactylaria, Drechslera, Embellisia, Exserohilum, Fusarium, Helminthosporium, Microsporum, Scolecobasidium and Scopulariopsis*. Pasarell et al teach that the culture antigens were incubated and aerated on a rotating shaker (p. 1655, 2nd column). Pasarell et al teach that the concentrated culture filtrate antigens was used to immunize two New Zealand White female rabbits. Pasarell et al teach that an emulsion of 1 ml of each control antigen and 1 ml of Freund incomplete adjuvant was injected intramuscularly into the New Zealand rabbits. *Alternaria, Dactylaria, Drechslera, Embellisia, Fusarium, Micosporum, Scolecobasisum and Scolecobasidium and Scopulariopsis* did not have common antigens when tested against the antisera. Antigens of *Helminthosporium* only reacted with its own sera and there were no cross-reactions with any other antigens tested (p. 1656, 1st column). Pasarell et al teach that antisera prepared from *E. rostratum* recognized antigens prepared from *E. holmii*. Pasarell et al teach that a similar result was observed with antisera prepare from *E. mcginnisii* and *E. longirostratum*. Pasarell et al that common antigens are shared between the genera of *Bipolaris* and *Curvularia* (p. 1656). The process limitation of the supernatant being prepared and used at 20°C is a matter of design choice. Although the reference appears to disclose the same cell culture supernatant claimed by the Applicants, the reference does not disclose the cell culture supernatant being prepared at the same temperature as the claimed process. However, the production of a cell culture supernatant by a particular process does not impart novelty or unobviousness to a cell culture supernatant when the same cell culture supernatant is taught in the prior art. This particularly true when properties of the cell culture supernatant are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). The fungal or yeast culture of Pasarell, et al appears to be the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's fungal or yeast culture supernatant with the fungal or yeast culture supernatant of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e., that the fungal or yeast culture supernatant of the prior art does not possess the same material structural and functional characteristics of the claimed fungal or yeast culture supernatant). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that the claims have been amended to distinguishing features over the cited prior art.

Applicant's arguments filed October 7, 2002 have been fully considered but they are not persuasive. It is the Examiner's position that there is nothing on the record to show that the fungal cell supernatant of the prior art is not the same as the claimed fungal cells. Claims 30-36, 40-41 and 45-46 are directed to a fungal or yeast cell supernatant as antigenic source for detecting level of antibodies from a sample test subject said fungal cell culture supernatant containing fungal components shed in to the supernatant during culturing. Pasarell et al teach concentrated culture filtrate antigens that were obtained from the genera *Alternaria, Bipolaris, Curvularia, Dactylaria, Drechslera, Embellisia, Exserohilum, Fusarium, Helminthosporium, Microsporum, Scolecobasidium and Scopulariopsis.* Pasarell et al teach that the culture antigens were incubated and aerated on a rotating shaker (p. 1655, 2nd column). Applicant has provided no side-by-side comparison to show that the fungal cell culture supernatant of the prior art differs from the claimed fungal cell culture supernatant. Therefore, the teaching of Pasarell et al anticipate the claimed invention.

6. The rejection under 35 U.S.C. 102(b) as anticipated by Calera et al is maintained for claims 30-35, 41 and 46 for the reasons set forth on pages 8-10, paragraph 6 of the previous Office Action.

The rejection was on the grounds that Calera et al teach cell culture supernatants obtained from *Aspergillus* (see the Abstract and page 2324). Calera teach that *Aspergillus nidulans* antigens elicit antibodies in rabbits. Calera et al teach that the *Aspergillus nidulans* antigens cross-reacted with antigens from *A. fumigatus, A. flavus, A. terreus, A. clavatus* and *A. niger* (p. 2331). Calera et al teach that screening a

battery of 10 selected human serum samples from patients with aspergilloma or invasive aspergillosis demonstrated that two antigens from stationary-phase culture supernatants were consistently reactive (see the Abstract). It would be inherent that the *Aspergillus* antigens would be effective in detecting aflatoxins since aflatoxins are obtained from microorganisms of the genera *Aspergillus*. The process limitation of the supernatant being prepared and used at 20°C is a matter of design choice. Although the reference appears to disclose the same cell culture supernatant claimed by the Applicants, the reference does not disclose the cell culture supernatant being prepared at the same temperature as the claimed process. However, the production of a cell culture supernatant by a particular process does not impart novelty or unobviousness to a cell culture supernatant when the same cell culture supernatant is taught in the prior art. This particularly true when properties of the cell culture supernatant are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). It would be inherent that the reference of the prior art would detect aflatoxins. The fungal or yeast culture of Calera, et al appears to be the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's fungal or yeast culture supernatant with the fungal or yeast culture supernatant of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e., that the fungal or yeast culture supernatant of the prior art does not possess the same material structural and functional characteristics of the claimed fungal or yeast culture supernatant). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that they disagree with Examiner's characterization of certain of the claim recitation do not define over the cited art. Applicant urges that Examiner's comments are not believed to be correct in view of the evidence provided in the specification.

Applicant's arguments filed October 18, 2002 have been fully considered but they are not persuasive. It is the Examiner's position that there is nothing on the record to show that the fungal cell supernatant of the prior art is not the same as the claimed fungal cells. Claims 30-35, 41 and 46 are directed to a fungal or yeast cell supernatant as antigenic source for detecting level of antibodies from a sample test subject said

fungal cell culture supernatant containing fungal components shed in to the supernatant during culturing. Calera et al teach cell culture supernatants obtained from *Aspergillus* (see the Abstract and page 2324), that *Aspergillus nidulans* antigens elicit antibodies in rabbits. Calera et al teach that the *Aspergillus nidulans* antigens cross-reacted with antigens from *A. fumigatus, A. flavus, A. terreus, A. clavatus* and *A. niger* (p. 2331) and that screening a battery of 10 selected human serum samples from patients with aspergilloma or invasive aspergillosis demonstrated that two antigens from stationary-phase culture supernatants were consistently reactive (see the Abstract). Applicant has provided no side-by-side comparison to show that the fungal cell culture supernatant of the prior art differs from the claimed fungal cell culture supernatant. Therefore, the teaching of Calera et al anticipate the claimed invention.

7. The rejection under 35 U.S.C. 102(e) as anticipated by Takesako et al is maintained for claims 30-35, 37-39, 41 and 45-46 for the reasons set forth on pages 10-11 paragraph 7 of the previous Office Action.

The rejection was on the grounds that Takesako et al teach the preparation of fungal antigens (i.e. *Candida albicans, Cryptococcus neoformans and Aspergillus fumigatus*). Takesako et al teach that the fungal antigens where suspended in Potato-Dextrose medium and subject to shaking overnight (column 27, lines 3-6). Takesako et al teach that *Candida* serum exhibited cross reactivity to proteins derived from *Cryptococcus neoformans* and *Aspergillus* (column 38, lines 25-28). Takesako et al teach that *Aspergillus* serum showed crossreactivity with *Cryptococcus* (column 38, lines 39-41). Takesako et al teach fungal antigen solutions that are mixed with equal volumes of incomplete Freund's adjuvant yield a water-in-oil vaccine preparation (column 28, lines 59-62). Limitations such as "the supernatant is prepared and used at 20°C" are viewed as a matter of design choice.

Since the Office does not have the facilities for examining and comparing applicant's fungal or yeast culture supernatant with the fungal or yeast culture supernatant of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e., that the

fungal or yeast culture supernatant of the prior art does not possess the same material structural and functional characteristics of the claimed fungal or yeast culture supernatant). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that the fungal antigens of the cited reference appear to be proteins and the Applicants have demonstrated in their specification that protease digestion of the claimed supernatants had minor effect on the antigen of the claimed invention. Applicant urges that the supernatants of the presently claimed invention are different from the cited art and the cited prior art fails to teach each and every aspect of the presently claimed invention. Applicant urges that the claimed antigens are soluble supernatants antigens and the antigens of Takesako et al are insoluble antigens. Applicant urges that Takesako et al appear to have enhanced immunogenicity of their preparations by using immunostimulants such as Freund's incomplete adjuvant and cholera toxin which were not required by the presently described methods. Applicant urges that the insoluble antigens of Takesako et al were suspended in Potato-Dextrose medium and the insoluble antigens of Takesako et al are quite different from the presently claimed invention.

Applicant's arguments filed October 18, 2002 have been fully considered but they are not persuasive. It is the Examiner's position that there is nothing on the record to show that the fungal cell supernatant of the prior art is not the same as the claimed fungal cells. Claims 30-35, 37-39, 41 and 45-46 are directed to a fungal or yeast cell supernatant as antigenic source for detecting level of antibodies from a sample test subject said fungal cell culture supernatant containing fungal components shed in to the supernatant during culturing. Takesako et al teach the preparation of fungal antigens

(i.e. *Candida albicans, Cryptococcus neoformans and Aspergillus fumigatus*). The Examiner disagrees with Applicants assertion that the claimed antigens are soluble supernatants antigens and the antigens of Takesako et al are insoluble antigens. Applicant is directed to column 7, lines 7-10 of the Takesako et al patent were it states "The present invention has also clarified that a "solubilized" fraction using a solubilizer such as a surfactant also processes potent antigenicity and the potent activity as vaccines". The Applicant is also directed to column 12, lines 43-45 which states "the solubilized fraction mainly contains antigenic soluble proteins, in addition to sugars and lipids". Therefore, Takesako et al teach soluble antigens. There is no requirement in the claims that the claimed vaccine should not comprise immunostimulants such as Freund's incomplete adjuvant and cholera toxin. Applicant has provided no side-by-side comparison to show that the fungal cell culture supernatant of the prior art differs from the claimed fungal cell culture supernatant. Therefore, the teaching of Takesako et al anticipate the claimed invention.

8. The rejection under 35 U.S.C. 102(b) as anticipated by van der Heide et al is maintained for claims 30-36, 41-42, 45-46 and newly presented claims 47-51 for the reasons set forth on pages 14-15, paragraph 10 of the previous Office Action.

The rejection was on the grounds that van der Heide et al teach *Aspergillus fumigatus*, *Penicllium notatum*, *Alternaria alternata* and *Cladosporium herbarum* antigenic extracts (see the Abstract and page 593, 1st column). van der Heide et al teach that 3 rabbits were immunized (1 rabbit per fungus) with an antigen mixture in Freund's adjuvant (page 593). It would be inherent that the *Aspergillus* antigens would be effective in detecting aflatoxins since aflatoxins are obtained from microorganisms of the genera *Aspergillus*. Limitations such as "the supernatant is prepared and used at a temperature above freezing" and the supernatant is prepared and used at 20°C"are

viewed as limitation of design choice. The limitation of detecting level of antibodies from a sample test subject" is a limitation of intended use.

Since the Office does not have the facilities for examining and comparing applicant's fungal culture supernatant with the fungal culture supernatant of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e., that the fungal culture supernatant of the prior art does not possess the same material structural and functional characteristics of the claimed fungal culture supernatant). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that van der Heide et al teach mycelial antigens or more specifically "somatic antigens (M) which will be excluding supernatant antigens as included in the claimed invention.

Applicant's arguments filed October 18, 2002 have been fully considered but they are not persuasive. It is the Examiner's position that there is nothing on the record to show that the fungal cell culture supernatant of the prior art is not the same as the claimed fungal cell culture supernatant. Applicant is directed to page 595 (bottom) were van der Heide et al teach antigens obtained from culture fluid. Therefore, van der Heide et al anticipates the claimed invention.

New Grounds of Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 43 is rejected under 35 U.S.C. 102(b) as anticipated by Pasarell et al *(Journal of Clinical Microbiology, July 1990, p. 1655-1657).*

Claim 43 is drawn to a fungal cell culture supernatant of *Biopolaris* displaying antigenicity towards antibody detection in a serodiagnostic assay for fungal antibody which comprises preparing said *Biopolaris* fungal cell culture supernatant reacting said fungal cell culture supernatant with sera from a test subject and determining the serum antibody level of said test subject.

Pasarell et al teach concentrated culture filtrate antigens that were obtained from the genera *Bipolaris*. Pasarell teach that reference antisera was tested by a microimmuodiffusion method against concentrated filtrates including *Bipolaris spp*. Pasarell et al teach that cross-reactivity was shown between isolates of the genera *Biopolaris* and *Curvularia*. Cross-reactivity was also seen among the different species of *Bipolaris*.

Since the Office does not have the facilities for examining and comparing applicant's fungal culture supernatant with the fungal culture supernatant of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e., that the fungal culture supernatant of the prior art does not possess the same material structural and functional characteristics of the claimed fungal culture supernatant). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Status of Claims

10. Claims 44 and 52-53 appear to be free of the cited prior art.

Conclusion

11. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
January 6, 2002

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